Remarks/Arguments

Claims 1-20 are pending. Claims 1-10 stand withdrawn as drawn to non-elected subject matter. In an Office Action mailed on October 16, 2006, the Office rejected claims 11-16 and 18, and objected to claim 17.

Claim Amendments:

Claims 11, 13, 14, and 15 have been amended for clarity and to present the claims in better form. No new matter has been added to these claims.

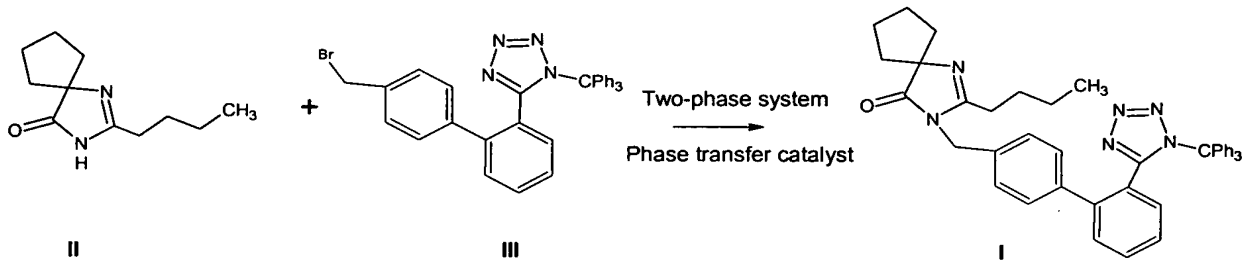
Claims 19 and 20 have been added. These claims are supported on page 4, lines 7-10.

Claim Rejections under 35 U.S.C. § 103(a):

Claims 11-16 and 18 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. patent No. 5,270,317 ("'317 patent") in view of International publication No. WO 99/38847 ("WO '847") for the reasons set forth on pages 3-7 of the Office Action. Applicants respectfully traverse.

Claims 11-16 and 18 recite processes for preparing irbesartan via the intermediate 2-butyl-3-[2'-(triphenylmethyl tetrazol-5-yl)-biphenyl-4-ylmethyl]-1,3-diazaspiro[4.4]non-1-ene-4-one ("Compound I"). The claims recite that the intermediate Compound I is prepared by reacting 2-butyl-1,3-diaza-spiro[4.4]non-1-ene-4-one ("Compound II") and 5-(4'-bromomethylbiphenyl-2-yl)-1-trityl-1H-tetrazole ("Compound III") in the presence of a phase transfer catalyst in a reaction system comprising organic and aqueous phases, as depicted in Scheme I below.

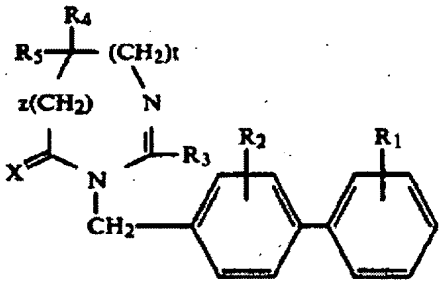
Scheme I: Process for Preparing Compound I



II III I

The trityl group on the tetrazole ring of Compound I is then removed to obtain irbesartan.

The '317 patent discloses a class of intermediates of irbesartan of the following formula:

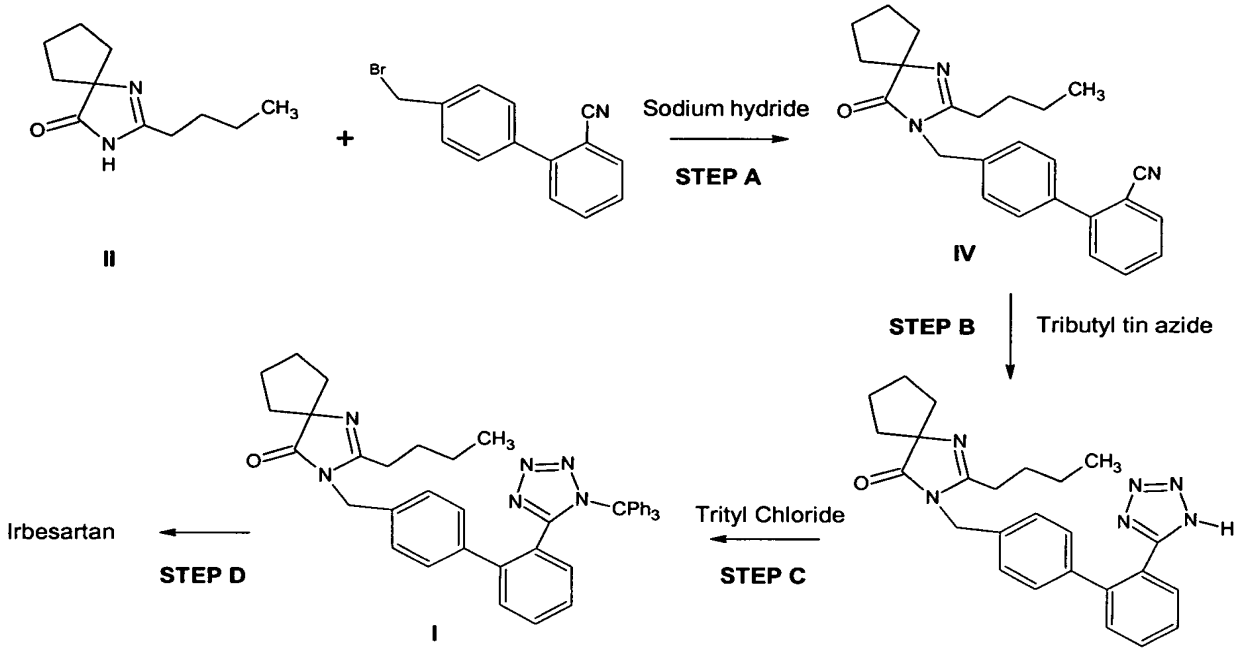


wherein R_1-R_5 can be selected from many different groups. '317 patent, col. 1, l. 38 to col. 2, l. 43. The '317 patent discloses that preferred intermediates are those in which R_1 is in the ortho position and is a carboxyl or tetrazoyl group and R_2 is hydrogen. *Id.* at col. 3, ll. 12-14.

The '317 patent discloses that these intermediates can be prepared by the reaction of a 2-alkyl-4-spirocyclopentane-2-imidazolin-5-one with a (biphenyl-4-yl)halomethyl derivative in a basic medium, such as potassium hydroxide, a metal alcoholate, a metal hydride, calcium carbonate, or triethylamine, in the presence of an inert solvent, such as dimethylformamide, dimethylsulfoxide, or tetrahydrofuran. *Id.* at col. 3, l. 53 to col. 4, l. 44; col. 9, ll. 54-58.

The '317 patent also discloses a specific process for preparing irbesartan by the following Scheme II. *See* '317 patent, col. 21, ll. 1-42 (examples 5(b) and (c)).

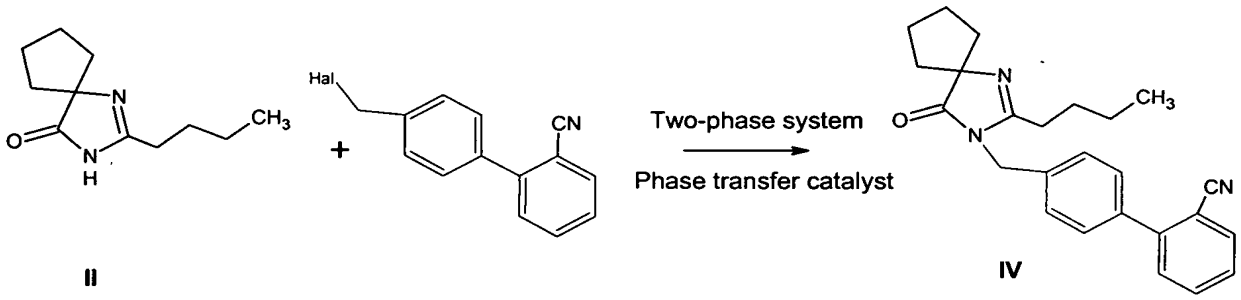
Scheme II: Process disclosed in the '317 patent



The '317 patent does not disclose the use of a phase transfer catalyst in preparing Compound I.

WO '847 discloses a process for preparing 4'-[[2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl][1,1'-biphenyl]-2-carbonitrile ("Compound IV"), an intermediate of irbesartan, by the reaction of Compound II above with a 4'-(halomethyl)[1,1'-biphenyl]-2-carbonitrile in the presence of a phase transfer catalyst. WO '847, p. 5, l. 5 to p. 6, l. 11. The process is depicted in Scheme III below.

Scheme III: Process disclosed in WO '847



WO '847 further discloses that the intermediate Compound IV may be converted into irbesartan by the process disclosed in the '317 patent. *Id.* at p. 1, ll. 27-33. WO '847 does not disclose the synthesis of Compound I.

The primary reference, the '317 patent, differs from the recitations of claims 11-16 and 18 at least in that it does not disclose the reaction of Compounds II and III in a biphasic system in the presence of a phase transfer catalyst. For example, Applicants' use of a biphasic system and a phase transfer catalyst eliminates the need for a strong base. Applicants' process allows one to employ milder bases that are more environmentally friendly, and, thus, more suitable for use on an industrial scale.

The secondary reference, WO '847, cannot remedy the deficiencies of the '317 patent. WO '847 discloses the use of a phase transfer catalyst to catalyze the reaction of Compound II and a 4'-(halomethyl)[1,1'-biphenyl]-2-carbonitrile to form the intermediate Compound IV, and not the intermediate Compound I. WO '847 does not teach or suggest that it would be desirable or even feasible to use a phase transfer catalyst to catalyze the reaction of Compounds II and III to form the intermediate Compound I, as recited in the claims.

Intermediate Compounds I and IV differ in the substitution of a trityl-protected tetrazole group for a cyano group. WO '847 does not teach or suggest such a substitution. In fact, WO '847 only discusses the substitution of the butyl group on Compound IV with other alkyl groups or alkoxy groups and does not teach or suggest any substitution for the cyano group. Advantageously, by starting with intermediate Compound I, the method of the

invention bypasses the intermediate Compound IV, thereby eliminating steps A, B, and C of the processes of the '317 patent and WO '847 (depicted in Scheme II above). This reduction in the number of process steps allows for a more streamlined process for preparing irbesartan that is more suitable for use on an industrial scale. Thus, the disclosures of WO '847, in combination with those of the '317 patent, would not motivate one of skill in the art to modify the disclosed process to produce Compound I, rather than Compound IV, through the use of a phase transfer catalyst, as recited in the claims. Accordingly, the rejection of claims 11-16 and 18 under 35 U.S.C. § 103(a) as obvious over the '317 patent in view of WO '847 cannot stand and should be withdrawn.

Claim 17 stands objected to as being dependent upon a rejected base claim. The Office states that this claim "would be allowable if written in independent form." Office Action, p. 7. Applicants defer rewriting claim 17 in independent form until a final decision on the patentability of claim 15 is made.

Conclusion:

In view of the foregoing remarks, Applicants respectfully submit that the claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If any outstanding issues remain, the examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Kenyon & Kenyon, LLP Deposit Account No. 11-0600.

Respectfully submitted,

KENYON & KENYON LLP

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